The immune system has evolved in such a way that it is capable of specifically distinguishing between self and non-self structures. Combining this with the ability to memorize and strongly prepare for all pathogens that it has previously encountered, is essential for the proper and effective function of the immune system, and provides the cornerstone for vaccine design. In all vertebrate animals, CD8+ cytotoxic T lymphocytes (CTLs) survey the intracellular environment for signs of invasion by pathogenic organisms such as viruses and bacteria. CTLs survey major histocompatibility complex (MHC) class I molecules, which are highly polymorphic peptide receptors which select and present endogenously derived peptides to circulating CTLs. Peptides that are recognized by CTLs in the context of MHC are epitopes, and represent a small sample of the pathogen proteome, making it possible for the immune system to specifically identify and react upon non-self peptide fragments unique only to the foreign intruder. The polymorphism of the MHC molecule effectively individualizes the immune response of each member of any given species. Moreover, responding T cells recognize antigen ligands, only in the context of peptide:MHC:β2m (pMHC) complex.

The gene encoding the MHC is one of the most polymorphic regions of the genome known. Despite thousands of different human leukocyte antigen (HLA) variants identified, each member of a species only inherits and expresses a few of these MHC alleles. The “MHC fingerprint” of an individual can be identified by defining MHC alleles. This is classically called “tissue typing” and is done by analyzing the reactivity of peripheral blood cells with sera unique to MHC alleles. Such knowledge is paramount to analysis of the immune response regarding MHC restriction and CTL recognition of pathogen-specific proteins.

Most of the polymorphism of MHC proteins is resident in the peptide binding groove. Hence, each MHC is unique in the way it binds peptides, and by inference it individualizes the entire T cell repertoire of the host. In this way, the diversity of MHC within a species makes immune escape almost impossible for any intruding pathogen.

Characterization of the SLA class I and class II gene products and their peptide binding capacity defines the T cell epitopes of any given pathogen proteome. To date the analysis of MHC peptide interactions, strength (affinity) and stability of the peptide:MHC complex, has been extensively reported in mice and humans, whereas data for livestock animals such as the pig is rather limited. This thesis describes adapting and applying analytical approaches, originally developed for man and mice to understand porcine MHC class I peptide binding characteristics in relation to immune responses to vaccination or infection. Applying proven technologies to newly produced, recombinant swine leukocyte antigen (SLA) class I proteins yielded a body of data for peptide:SLA:β2m (pSLA) complex affinity and stability.

Mapping the SLA proteins for their peptide binding requirements along with the identification of their cognate virally derived peptides, made it possible to explore the nature of the SLA proteins and the roles they play in establishing adaptive immunity. The development of SLA tetramers, enabled investigation of the specific CTL response elicited as a result of immunization against foot-and-mouth-disease virus (FMDV) and swine influenza A virus. These studies resulted in the identification of T cell epitopes from both viruses.

As SLA:peptide binding data accumulates in these and similar studies, it becomes possible for collaborators at Center for Biological Sequence Analysis (CBS), DTU, to further strengthen the NetMHCpan algorithm. This prediction tool now has the capacity for the selection of peptide candidates to be bound by human (HLA), bovine (bovine leukocyte antigen (BoLA)) and swine (SLA) MHC proteins.

Expanding the knowledge of porcine MHC class I molecules, mapping their peptide binding matrices, and producing tetramers as well as improving today’s state-of-the-art method for SLA peptide prediction will modernize immunological science of livestock species. These approaches and results should lead to accelerated development of vaccines with increased efficacy due to optimal activation of cell-mediated immune responses with minimal adverse events.

**General information**

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